

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

INTEGRATED DNA TECHNOLOGIES, INC.,
Petitioner,

v.

TECAN GENOMICS, INC.,
Patent Owner.

IPR2024-01504
U.S. Patent 11,098,357

PETITIONER'S REPLY

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EXHIBIT LIST

Exhibit	Short Name	Document
Ex. 1001		Reserved
Ex. 1002		Reserved
Ex. 1003	'399 patent	U.S. Patent No. 9,546,399
Ex. 1004	'357 patent	U.S. Patent No. 11,098,357
Ex. 1005	'241 patent	U.S. Patent No. 11,725,241
Ex. 1006		Reserved
Ex. 1007	Siebert	Siebert et al., <i>An improved PCR method for walking in uncloned genomic DNA</i> , Nucleic Acids Res. 23(6) 1087–1088 (1995)
Ex. 1008	Caruccio	Caruccio, <i>Preparation of Next-Generation Sequencing Libraries using Nextera™ Technology: Simultaneous DNA Fragmentation and Adaptor Tagging by In Vitro Transposition</i> , High-Throughput Next Generation Sequencing: Methods and Applications, Methods in Molecular Biology, Ch. 17 (2011)
Ex. 1009	Bronner	Bronner et al., <i>Improved Protocols for Illumina Sequencing</i> , Curr Protoc Hum Genet. (2009)
Ex. 1010		Reserved
Ex. 1011	Iafrate	U.S. Patent Application Publication No. 2013/0303461
Ex. 1012	Kivioja	Kivioja et al., <i>Counting absolute numbers of molecules using unique molecular identifiers</i> , Nature Methods (2011)
Ex. 1013	Bielas	International Publication No. WO 2013/123442 A1
Ex. 1014	Masoudi-Nejad	Masoudi-Nejad et al., <i>Next Generation Sequencing and Sequence Assembly Methodologies and Algorithms</i> (2013)

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Ex. 1015	Zheng	Zheng et al., <i>Anchored multiplex PCR for targeted next-generation sequencing</i> , Nature Medicine (2014)
Ex. 1016		Reserved
Ex. 1017		Reserved
Ex. 1018		File History for U.S. Patent No. 9,546,399
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Ex. 1020		File History for U.S. Patent No. 11,725,241
Ex. 1021	Miner	Miner et al., <i>Molecular barcodes detect redundancy and contamination in hairpin-bisulfite PCR</i> , Nucleic Acid Research 32:17 (2004)
Ex. 1022	McCloskey	McCloskey et al., <i>Encoding PCR Products with Batch-stamps and Barcodes</i> , Biochem Genet 45:761–767 (2007)
Ex. 1023	Hiatt	Hiatt et al., <i>Parallel, tag-directed assembly of locally derived short sequence reads</i> , Nat Methods 7(2):119–122 (2010)
Ex. 1024	König	König et al., <i>iCLIP reveals the function hnRNP particles in splicing at individual nucleotide resolution</i> , Nat Struc Mol Biol. 17(7):909–915 (2010)
Ex. 1025	Kinde	Kinde et al., <i>Detection and quantification of rare mutations with massively parallel sequencing</i> , PNAS 108(23):9350–9535 (2011)
Ex. 1026	Casbon	Casbon et al., <i>A method for counting PCR template molecules with application to next-generation sequencing</i> , Nucleic Acids Research 39:12 (2011)

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Ex. 1027	Fu	Fu et al., <i>Counting individual DNA molecules by the stochastic attachment of diverse labels</i> , PNAS 108(22):9026–9031 (2011)
Ex. 1028	Jabara	Jabara et al., <i>Accurate sampling and deep sequencing of the HIV-1 protease gene using a Primer ID</i> , PNAS 108(50):20166–20171 (2011)
Ex. 1029	Tollervey	Tollervey et al., <i>Characterising the RNA targets and position-dependent splicing regulation by TDP-43; implications for neurodegenerative diseases</i> , Nat Neurosci. 14(4):452–458 (2011)
Ex. 1030	Shiroguchi	Shiroguchi et al., <i>Digital RNA sequencing minimizes sequence-dependent bias and amplification noise with optimized single-molecule barcodes</i> , PNAS 109(4):1347–1352 (2012)
Ex. 1031	Schmitt	Schmitt et al., <i>Detection of ultra-rare mutations by next-generation sequencing</i> , PNAS 109(36):14508–14513 (2012)
Ex. 1032	De Luca	De Luca and Dono, <i>The Opportunities and Challenges of Molecular Tagging Next-Generation Sequencing in Liquid Biopsy</i> , Molecular Diagnosis & Therapy 25:537–547 (2021)
Ex. 1033	Samuels	U.S. Patent Application Publication No. 2012/0220494
Ex. 1034		Reserved
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Ex. 1037		Reserved
Ex. 1038		Reserved
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Ex. 1040		Reserved
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Ex. 1048		U.S. Provisional Patent Application 61/645,364
Ex. 1049		U.S. Provisional Patent Application 61/679,302
Ex. 1050	Moorthie	Moorthie et al., <i>Review of massively parallel DNA sequencing technologies</i> , HUGO Journal 5:1–12 (2011)
Ex. 1051		Reserved
Ex. 1052		Reserved
Ex. 1053	Syed	Syed, <i>Chapter 19: Second-Generation Sequencing Library Preparation: In Vitro Tagmentation via Transposome Insertion</i> , in <i>Tag-Based Next Generation Sequencing</i> (Matthias Harbers and Günter Kahl, eds., 2011)
Ex. 1054	Loeb	Loeb et al., <i>Transcriptome-wide miR-155 Binding Map Reveals Widespread Noncanonical MicroRNA Targeting</i> , Molecular Cell 760–770 (2012)
Ex. 1055	Kircher	Kircher et al., <i>Double indexing overcomes inaccuracies in multiplex sequencing on the Illumina platform</i> , Nucleic Acids Research 40:1 (2012)
Ex. 1056	Illumina Letter	Illumina Customer Letter (Sept. 7, 2012)
Ex. 1057	Nextera Prep Guide	Nextera® XT DNA Sample Preparation Guide (Oct. 2012)

Exhibit	Short Name	Document
Ex. 1058	Troutt	Troutt et al., <i>Ligation-anchored PCR: A simple amplification technique with single-sided specificity</i> , PNAS, USA 9823–9825 (1992)
Ex. 1059	Hug & Schuler	Hug and Schuler, <i>Measurement of the Number of Molecules of a Single mRNA Species in a Complex mRNA Preparation</i> , J. Theor. Biol. 221:615–624 (2003),
Ex. 1060	Meyer & Kircher	Meyer and Kircher, <i>Illumina Sequencing Library Preparation for Highly Multiplexed Target Capture and Sequencing</i> , Cold Spring Harbor Protocols (2010)
Ex. 1061	Kircher Thesis	Kircher Thesis, <i>Understanding and improving high-throughput sequencing data production and analysis</i> , Leipzig University, Germany (2011)
Ex. 1062	Smith Thesis	Smith Thesis, <i>Low-Level Variant Detection in Human Mitochondrial DNA Using The Illumina® MiSeq™ Next-Generation Sequencing (NGS) Platform</i> , Western Carolina University (2013)
Ex. 1063	Won	Won et al., <i>Detecting Somatic Genetic Alterations in Tumor Specimens by Exon Capture and Massively Parallel Sequencing</i> , J. Visualized Experiments (2013)
Ex. 1064	Kozich	Kozich et al., <i>Development of a Dual-Index Sequencing Strategy and Curation Pipeline for Analyzing Amplicon Sequence Data on the MiSeq Illumina Sequencing Platform</i> , Applied and Environmental Microbiology 79:17, 5112–5120 (2013)

Exhibit	Short Name	Document
Ex. 1065	Pray	Pray, <i>Major Molecular Events of DNA Replication</i> , Nature Education (2008)
Ex. 1066	Mackenzie	Mackenzie, <i>DNA vs. RNA – 5 Key Differences and Comparison</i> , Technology Networks (2020)
Ex. 1067	Clancy	Clancy and Brown, <i>Translation: DNA to mRNA to Protein</i> , Nature Education (2008)
Ex. 1068	Gauthier Thesis	Gauthier Thesis, <i>Simulation of polymer translocation through small channels</i> , University of Ottawa, Canada (2008)
Ex. 1069	Lohman	Lohman et al., <i>DNA Ligases</i> , Current Protocols in Molecular Biology 3.14.1-3.14.7 (2011)
Ex. 1070	Margulies	Margulies et al., <i>Genome sequencing in microfabricated high-density picolitre reactors</i> , Nature 376–380 (2005)
Ex. 1071		DNA Sequencing Costs: Data, https://www.genome.gov/about-genomics/fact-sheets/DNA-Sequencing-Costs-Data
Ex. 1072	Craig	Craig et al., <i>Identification of Genetic Variants Using Barcoded Multiplexed Sequencing</i> , Nat. Methods 5(10) 887–893 (2008)
Ex. 1073	Parameswaran	Parameswaran et al., <i>A pyrosequencing-tailored nucleotide barcode design unveils opportunities for large-scale sample multiplexing</i> , Nucleic Acids Research 35:19 (2007)
Ex. 1074	Lonigro	Lonigro et al., <i>Detection of Somatic Copy Number Alterations in Cancer Using Targeted Exome Capture Sequencing</i> , Neoplasia 13(11) 1019–1025 (2011)

Exhibit	Short Name	Document
Ex. 1075	Bielas Annotated Figure	Annotated Figure
Ex. 1076	Bielas Illumina P5	Annotated Figure
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Ex. 1116		Bustamante Deposition Demonstrative—Claim Construction Scenario 3
Ex. 1117		Bustamante Deposition Demonstrative—Claim Construction Scenario 4
Ex. 1118		Bustamante Deposition Demonstrative—Claim Construction Scenario 4.1
Ex. 1119		Bustamante Deposition Demonstrative—Claim Construction Scenario 4.2
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Ex. 1121		Bustamante Deposition Demonstrative—Claim Construction Scenario 5
Ex. 1122		Bustamante Warren Report 2018
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Ex. 1124		Bustamante Deposition Transcript— Part I
Ex. 1125		Reserved
Ex. 1126		Reserved

INTRODUCTION

Claim 1 recites a method for “detecting duplicate sequencing reads.” EX1004 at 25:36-37. The petition detailed the nucleic acid chemistry of the first three limitations of claim 1 that concern the “physical” aspects of preparing a library and obtaining sequencing reads, *e.g.*, Paper 1 (“Pet.”) at 4-20; EX1124 at 26:8-28:20, and explained why these limitations were found in the prior art. Tecan addresses none of these limitations in its Response.

This dispute now focuses solely on how to interpret and apply the method’s final limitation: “identifying sequence reads with identical identifier and target sequences as duplicates.” This limitation relates to the analysis of sequencing data; in the words of Tecan’s expert, Dr. Carlos Bustamante, it is a “computer-aided” limitation. EX1124 at 27:21-28:20.

Tecan’s Response depends exclusively on new constructions of the “identifying” limitation of claim 1 and dependent claim 2’s related information-processing limitation that the method “remov[e] a duplicate read from the sequence reads.” But these limitations do not distinguish any of the asserted prior art, even under Tecan’s new constructions. The Petition explained why the Challenged Claims are anticipated by Bielas, EX1013 (or with respect to dependent claim 9,

obvious¹). The Bielas method first organizes sequencing reads by comparing their identifier sequences, then it compares target sequences. Tecan argues that by breaking up these sequence comparisons, Bielas does not teach a “step” of identifying duplicates. Paper 21 (“POR”) at 35-36. Even if the Board were to adopt Tecan’s proposal to read the word “step” into the identifying limitation, Dr. Bustamante agreed that a sequential analysis like that in Bielas constitutes a “step.” EX1124 at 52:1-54:10.

Tecan next contends that Bielas does not disclose the claimed method because the Bielas algorithm compares its sequences nucleotide-by-nucleotide and reduces them to a single consensus sequence. But the patent does not require any particular algorithm for how two sequences get compared and, if they match, get reduced to one. EX1124 at 171:9-172:20. Bielas therefore anticipates claims 1-4, 6-7, and 10.

¹ Ground 3 concerns the obviousness over Bielas of claim 9, which requires that the identifier sequence be eight nucleotides. The number of nucleotides is a design choice, Pet. at 68-69, which Tecan did not dispute, POR at 37-38, and which Dr. Bustamante confirmed, EX1124 at 144:5-145:7. Ground 3 also explained how Bielas rendered obvious claims 1-4, 6-7, and 10 even if Tecan disputed whether Bielas taught certain “physical” limitations, which Tecan did not.

Separately and independently, the Petition explained why the claims would have been obvious over the combination of a known sequencing method (Iafrate, EX1011) with a known technique for identifying duplicates in sequencing read data (Kivioja, EX1012). Tecan notably did not ask Dr. Bustamante to opine on whether the POSA would have wanted to combine these methods, EX1124 at 157:20-158:1, and thus the opinion of Dr. Sims, Petitioner's expert, that the POSA would have been motivated to do so is unrebutted.

Kivioja's sequence analysis method involved comparing sequencing reads to a known genome to obtain each sequencing read's genomic coordinates. It then compared those coordinates and the identifier sequences to identify duplicates. Tecan advances only the narrow argument that this workflow does not disclose "identifying sequence reads with identical identifier and target sequences as duplicates" because of how genomic coordinates were used. But it is undisputed that Kivioja's method used the target sequences, and it is undisputed that this is precisely the same method that is described in the patent's Example 1 and Figure 5 for identifying, in the patent's words, "'true' duplicates." EX1124 at 86:5-23.

None of these arguments distinguish the claimed methods from the prior art, and the Board accordingly should cancel claims 1-4, 6-7, and 9-10.

I. SEQUENCE ANALYSIS BACKGROUND

Because the dispute focuses entirely on the “identifying” limitation, this section highlights certain technical points relevant to the remaining disputes.

The Petition explained how 2010’s release of the Illumina HiSeq 2000 sequencer unleashed a torrent of scientific publications describing the use of molecular barcodes or “identifiers.” Pet. at 14-18; EX1079.¶¶113-169. Tecan did not comment on these articles, but acknowledged that the “barcode method” was known in the art. POR at 6. Dr. Bustamante agreed that the POSA already knew how to use molecular barcodes and that it was “a problem people were working on.” EX1124 at 143:17-144:4; EX2035.¶64.

The state of the art concerning sequence analysis also was well-developed. Dr. Bustamante’s declaration illustrated a typical workflow for processing sequencing data. EX2035.¶53. He confirmed that the POSA would have been familiar with this workflow and capable of re-organizing its modules to fit their needs. EX1124 at 138:2-139:2.

One of these standard workflow modules is known as “Reference Genome Alignment.” EX2035.¶¶53-59. Genomic alignment involves comparing the sequencing read to a reference genome. EX1124 at 139:15-140:16; *id.* at 80:10-81:9 (describing Bowtie genomic alignment program). The result of this comparison is the assignment of genomic coordinates to the sequencing read. *Id.* at 142:1-16.

Relatively short sequences aligned to the genome in this manner, for example, the 36-base reads generated in the patent's Example 1, "are nearly if not always identical" to the reference genome. EX1124 at 89:15-90:3, 90:25-91:14. In this manner, genomic coordinates convey sequence information.

Another standard workflow module is "duplicate identification." EX2035.¶53, ¶¶61-63. As the patent states, there were "[s]tandard PCR duplicate removal" software packages like "PICARD, Markduplicates, and[] SAMtools rmdup" that were available to the POSA. EX1004 at 18:38-40. Dr. Bustamante confirmed that these software packages "were available at the time" and "part of many workflows." EX1124 at 91:20-95:1. As Dr. Bustamante explained, "people have been using software to analyze DNA sequences for a long time," *id.* at 94:20-95:1, and "identifying duplicates was a long-standing problem in the field," *id.* at 143:9-15.

A third form of computer-aided sequence analysis known in the art is the generation of a "consensus sequence." As Dr. Sims explained, a consensus sequence "is a sequence that one arrives at by analyzing multiple reads and then making a judgment as to what the correct sequence of the originating nucleic acid fragment likely is." EX2016 at 101:12-15; *see also* EX2035.¶124; EX2003.0037; EX2004.0014. Or, as Dr. Bustamante explained in his deposition, it is a sequence generated by comparing multiple sequences "character by character by character one

character at a time and selecting the most common character at each position.”

EX1124 at 62:14-65:17.

II. CLAIM CONSTRUCTION

In its Institution Decision, the Board invited the parties to address the proper construction of (1) “duplicates,” (2) “identifying sequence reads with identical identifier and target sequences as duplicates,” and (3) “comprising.” Paper 7 (“ID”) at 11-13. The parties agree on issues (1) and (3). But as to the “identifying” limitation, Tecan’s proposal does not illuminate the meaning of the claim, it simply adds words to it that are not there. Those insertions should be rejected.

A. “Duplicates” Require 100% Identity Between Two Sequences.

Claim 1 provides that “duplicates” are “sequence reads with *identical* identifier and target sequences.” EX1004 at 25:46-47 (emphasis added). There is no dispute that the term “duplicates” as used in the patent requires the sequences to be identical. *See* POR at 16-17; EX1124 at 31:1-38:3 (discussing demonstratives EX1113, EX1114, and EX1115). Requiring a “duplicate” to be 100% identical, i.e., having a Hamming distance of zero, EX1124 at 37:24-38:3, accords with the plain and customary meaning of “identical” as used in the claim. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (en banc).

B. The Board Should Not Add Words to “Identifying Sequence Reads with Identical Identifier and Target Sequences As Duplicates.”

Claim 1’s identifying limitation reads “identifying sequence reads with identical identifier and target sequences as duplicates.” The redline text below reveals how Tecan has simply asked the Board to add words to the claim. *See* POR at 9-15:

Tecan’s Proposed Construction	Petitioner’s Proposed Construction
“identifying sequence reads <u>as duplicates</u> through a step that uses both with-identical the identifier and at least a portion of the target sequences ~~as~~ <u>duplicates</u> ”	“identifying sequence reads with identical identifier and target sequences as duplicates.” This limitation requires the entire “target sequence” and does not require a single “step.”

The Board should reject Tecan’s invitation to rewrite the claim and instead give the claim its plain and customary meaning without Tecan’s insertions: “identifying sequence reads with identical identifier and target sequences as duplicates” does not impose any temporal limitation (“a step”) and is not satisfied by comparison of less than the entirety of the target sequence (“at least a portion of”). *Phillips*, 415 F.3d at 1312-13.

1. Tecan’s Addition of “a Step” is Unwarranted and Provides No Additional Substance.

The phrase “a step” is not in claim 1. EX1004 at 25:36-47. Yet Tecan inserts it and argues that “identifying sequence reads with identical identifier and target

sequences as duplicates” must occur in *a single step* that “us[es] both the identifier and ... the target sequence” *at the same time*, POR at 10-15, 34.

The Board cannot “broaden [] or narrow claims to give the patentee something different than what he has set forth.” *Tex. Instruments Inc. v. ITC*, 988 F.2d 1165, 1171 (Fed. Cir. 1993) (quotation omitted). And what claim 1 sets forth does not limit how the “identifying” limitation is performed. EX1004 at 25:46-47; EX1124 at 171:2-172:20. Neither the claim’s plain language nor the specification supports Tecan’s proposed temporal limitation;² rather, the identifying limitation requires only that both pieces of sequence information—identifier and target sequence—be used in the data analysis.

Tecan argues that “[e]ach of the steps of the claimed method include specific elements necessary for that step” and that this supports a temporal limitation. POR

² The only temporal limitation supported by the claim language is that the identification of duplicates must be practiced after the preceding limitations in claim 1. But that does not require that the identifier site and target sequence must be used simultaneously. The identifying limitation is descriptive of what must be identical for two sequences to be duplicates: duplicates have “identical identifier and target sequences.” EX1004 at 25:46-47. There is no limit on *when* or *how* in the process of identifying duplicates such information must be used.

at 10. But certain limitations that precede the identifying limitation are themselves multistep processes—for example, “amplifying” and “sequencing.” EX1004 at 25:43-45. As the ’357 patent explains, “amplifying” is typically done by PCR. *Id.* at 5:54. PCR is not a single, independent step. Rather, PCR is a series of steps: denaturing, annealing, generating a complement strand, and repeating. EX1079.¶¶68-70; EX2035.¶38. Likewise, “sequencing” is a multistep process. EX1004 at 12:61-13:5 (sequencing occurs in “cycles,” “one base at a time”).

Thus, contrary to Tecan’s assertion, the limitations preceding the identifying limitation do not support the idea that duplicates must be identified by identical identifier and target sequences in a single data analysis step. The Board should not add to claim 1 a limitation on *when* identifier and target sequence are used in the data analysis because it is unsupported by the claim’s plain language. *See Apple Inc. v. Gesture Tech. Partners, LLC*, 129 F.4th 1367, 1380 (Fed. Cir. 2025) (rejecting addition of temporal limitation that was not in claim language); *Hoganas AB v. Dresser Indus., Inc.*, 9 F.3d 948, 950 (Fed. Cir. 1993) (rejecting addition of a size limitation where language of the claim was about shape).

Tecan’s proposed construction also is not supported by the specification. Tecan cites Example 5, EX1004 at 19:38-21:3, to argue that the identifying limitation has a temporal requirement, POR at 11-13, but that ignores every other teaching in the specification. For instance, Example 1 teaches a method of

deduplication where sequencing reads first underwent “alignment with bowtie aligner” so that “duplicate reads” could be “identified by their genomic start positions.” EX1004 at 17:39-43. Then the “sequencing reads that started at the same genomic position were checked against the random bases,” i.e., the identifier, “to see if they have the same or different set of random bases that were ligated to them.” *Id.* at 17:43-46. “Where two sequences with the same starting genomic coordinate had the same set of random bases,” they were deemed to be duplicates. *Id.* at 17:47-52. In other words, Example 1 teaches using the target sequence first to determine the sequencing read’s genomic coordinate, followed by the use of the identifier to finally determine “the number of true duplications versus the number of apparent or perceived duplicates.” *Id.* at 17:61-63.

The prosecution history also does not support Tecan’s proposed construction. Tecan cites the prosecution history of the now-disclaimed U.S. Patent No. 9,546,399, arguing that it overcame the Examiner’s rejections by amending claim 1 to include an identifying limitation that occurs in a single step. POR at 13-15; EX1018.0780-81, .0797-0807. Tecan argues similarly about the prosecution history of the ’357 patent. POR at 15; EX1019.0453.

The language Tecan points to is, at best, ambiguous. The use of the identifier “in combination” with or “in conjunction with” the target sequence, POR at 15, does not indicate that the identifier and target sequence be used in a single step; rather, it

means that both the identifier and target sequence must be used in the data analysis, without regard to the order of operations. Nor is it clear that “the active step,” POR at 14, means anything more than the step of identifying duplicates. Given that the prosecution history “neither support[s] nor discredit[s]” the meaning of the term, the Board should “decline to give the prosecution history much weight.” *See AquaTex Indus., Inc. v. Techniche Sols.*, 419 F.3d 1374, 1381 (Fed. Cir. 2005); *Phillips*, 415 F.3d at 1317. It certainly cannot justify rewriting the claims to add words that are not there.

Finally, Tecan’s proposed construction appears irrelevant given the testimony of Dr. Bustamante:

Q. Dr. Bustamante, how would you understand the meaning of step in your claim construction opinion?

A. Well, I would go back to the claims and say ***the step being performed here is identifying sequencing reads*** with identical identifier and target sequences duplicates and that requires you to have unique identifier and unique target sequence.

EX1124 at 51:15-22 (emphasis added), 45:3-54:10. In other words, “a step” is simply descriptive. The identifying limitation is part of the claimed method of identifying duplicate sequencing reads, just like the preceding limitations that require “ligating an adaptor” or “amplifying the adaptor-ligated fragments” or “sequencing the amplicons.” EX1004 at 25:37-45.

Under Dr. Bustamante’s understanding of the term, “a step” can encompass anything from identifying duplicate sequencing reads by looking at the entirety of the identifier and target sequences, to “string comparison,” or “character comparison,” on a nucleotide-by-nucleotide basis. EX1124 at 52:5-54:10. It “is all part of the single identifier step.” *Id.* at 54:3-4. Dr. Bustamante testified that no particular algorithm or software package is required to practice the identifying limitation. *Id.* at 96:15-98:3. In short, not even Dr. Bustamante understands the identifying limitation to be so narrow as to require the simultaneous use of identifier and target sequence when identifying duplicates.

2. “At Least a Portion” Is Not in the Claim.

“At least a portion” appears nowhere in the claim language. And Tecan does not defend this proposed addition in its brief. POR at 9-15. The Board should not rewrite the claim to add limitations. *Gesture*, 129 F.4th at 1380; *3M Innovative Properties Co. v. Tredegar Corp.*, 725 F.3d 1315, 1321 (Fed. Cir. 2013).

“At least a portion” loses all meaning under Tecan’s proposed construction. When asked about the meaning of “at least a portion,” Dr. Bustamante stated that “[a] single base by definition would be a portion of a target sequence.” EX1124 at 39:8-13; *see also id.* at 41:12-45:10. In other words, Dr. Bustamante submits that, under Tecan’s proposed claim construction, a *single base* could constitute “at least a portion of” the target sequence used in identifying sequence reads as duplicates.

Such a claim construction strains credulity and finds no support in any part of the '357 patent.

Moreover, Tecan's reading of Example 5 does not justify adding words that are not in the identifying limitation. Tecan suggests that because Example 5 teaches that "the first 50 bases of the target sequence are read and compared to each other," Example 5 uses only "a portion of the target sequence." POR at 11-12. But the sequencing read in Example 5 was the "50 base first read." EX1004 at 20:52-53; EX1124 at 99:21-23. Thus, Example 5 actually teaches what the claim language requires: using the entire target sequence of the sequencing read to identify duplicates. EX1004 at 25:46-47.

The prosecution history also does not support Tecan's claim construction. Dr. Bustamante contended the "[a]pplicants ... explained that this 'identifying' step required comparison of both the identifier *and a portion* of the target sequence," EX2035.¶92 (emphasis added). But the very language Dr. Bustamante points to, EX1018.0807, nowhere mentions "a portion":

d) ~~detecting~~ identifying a duplicate sequencing read as the population of sequencing reads comprising the same identifier site and nucleic acid fragment as another sequencing read in the population of sequencing reads ~~a sequencing read with a duplicate identifier site and target sequence;~~

The Board should not rewrite the claims as Tecan urges.

C. “Comprising” Allows for the Claimed Method to Identify Sequences Containing Mismatches.

The Board asked whether the “comprising” nature of claim 1 means “the prior art meets the claim if the prior art discloses a method of identifying as duplicates those sequence reads with identical labels and target fragments and, in addition also identifies other sequence reads as duplicates, including sequence reads with some mutations resulting from PCR or SBS error.” ID at 10, 13.

The parties agree that the answer is “yes.” Claim 1 allows for “identification of both duplicates,” i.e., sequences that are a 100% match, “and sequences that contain PCR and SBS errors.” POR at 18-19. No one contends that claim 1 would encompass “*only* identification of reads without duplicate sequences (those that contain PCR or SBS errors).” *Contra* POR at 18 (emphasis added). All claim 1 requires is that two sequences are identified as duplicates using the claimed method, even if the method identifies as duplicates additional sequences that are not 100% identical. *See, e.g.*, EX1124 at 55:11-57:3; EX1117.

III. GROUNDS II AND III: ANTICIPATION AND OBVIOUSNESS OVER BIELAS

Tecan disputes whether Bielas teaches the identifying limitation in claim 1 and deduplication as recited in claim 2. POR at 33-37; EX2035.¶¶117-124, ¶¶141-148. That leaves Dr. Sims’ opinion that Bielas teaches the remaining limitations of

claim 1 and the remaining dependent claims, EX1079.¶¶563-576, ¶¶581-609, un rebutted.

A. Claims 1 and 2 Are Anticipated By Bielas.

Tecan argues that because the objective of Bielas' method "is to determine if a mutation is an artifact of PCR or a true mutation in the sample" it does not teach the method of claims 1 and 2. POR at 36. The objective in Bielas is irrelevant—the anticipation inquiry "asks solely whether the prior art reference discloses" the claims, "not how the prior art characterizes that disclosure." *Hewlett-Packard Co. v. Mustek Sys., Inc.*, 340 F.3d 1314, 1324 n.6 (Fed. Cir. 2003). What matters is that Bielas' method disclosed each of the elements of claims 1 and 2 of the '357 patent. *See id.*

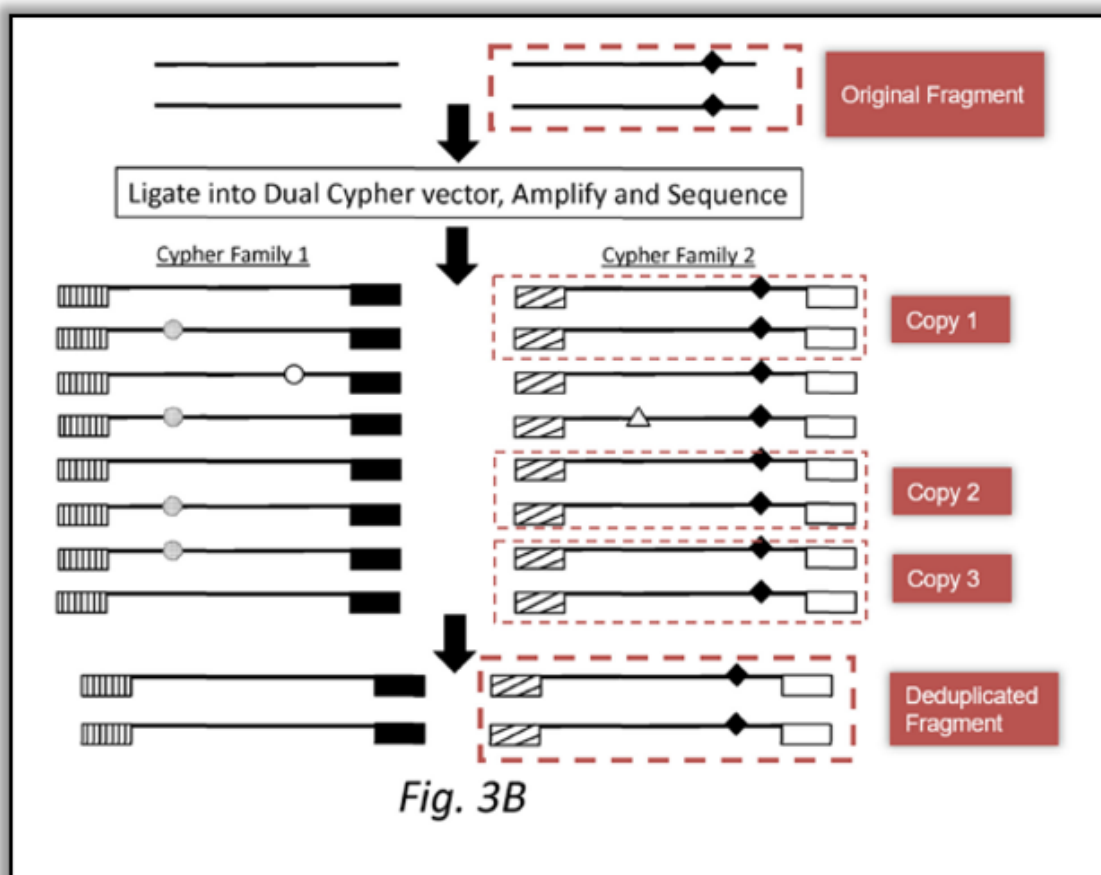
There is no dispute that Bielas' method in Example 3 obtained sequence reads with identifiers and target sequences, sorted those sequence reads by comparing identifiers, and then compared target sequences. EX1079.¶¶483-486; EX1124 at 163:5-166:24; 172:3-172:20. Because these events occurred in series, Tecan says Bielas does not disclose claim 1. POR at 34-37. But claim 1 does not require the identifier and target sequence be used in a single "step." *Supra* at 7-12. And even if the Board concludes otherwise, Bielas still disclosed the method of claim 1. As Dr. Bustamante explained, sequencing data can be analyzed character-by-character

or string-by-string, and however the algorithm divides up the comparison, it all constitutes a “step.” EX1124 at 52:1-54:10.

Tecan next disputes that Bielas discloses a method that “identifies duplicates.” Tecan is wrong. As discussed, *supra* at 14, because claim 1 is a comprising claim, its method “identifies” two sequences as duplicates (defined as 100% identical) even if it also identifies as a duplicate a sequence that contains PCR or sequencing errors. Dr. Bustamante testified that the following hypothetical, EX1117, practices claim 1 because “the first two sequences ... are identical and have been identified as duplicates by the method” described in claim 1—that is by using the identifier and target sequence. EX1124 at 56:23-57:1.

<u>Reads</u>		<u>De-duplication</u>	
5'	TAGATCGCATCCGTAAATTCGCGTAGGAATCAAATTGC	5'	TAGATCGCATCCGTAAATTCGCGTAGGAATCAAATTGC
5'	TAGATCGCATCCGTAAATTCGCGTAGGAATCAAATTGC		
5'	TAGATCGCATCCGTAAATTCGCGTAGGAATCAAATTGC		
5'	TAGATCGCATCCGTAAATTCGCGTAGGAATCAAATTGC		
	Unique IdentifierTarget Sequence		Unique IdentifierTarget Sequence

So too in Bielas. The righthand column of Bielas’ Figure 3B, EX1013.0043, reproduced below as annotated by Dr. Sims, EX1079.¶486, depicts three pairs of sequences that are identical and one pair with a sequencing error (represented as a triangle), EX1013.0006; EX1124 at 163:25-164:24.



In the final step depicted in Figure 3B, the sequence reads are collapsed into a consensus sequence. EX1013.0006. As Dr. Bustamante explained, “[t]he families are defined based on the combination of cyphers and then the consensus sequence is derived across the families for those that have common cypher combinations.” EX1124 at 161:9-13. Creating a consensus sequence can encompass the identification and removal of duplicates as described in the ’357 patent because it involves the character-by-character comparison of the sequence reads. *Supra* at 5-6; *see also* EX1124 at 170:3-172:20; *id.* at 60:9-73:7. Just as in EX1117, Figure 3B depicts deduplication of sequence reads that are 100% identical, EX1079.¶¶483-486,

even though it included in the analysis one sequence that was not, EX1013.0006, .0043; EX1124 at 170:3-172:20.

Tecan also raises an issue about Bielas' Example 1. In that method, Bielas stated that "the unique cypher tags are used to computationally deconvolute the sequencing data and map all sequence reads to single molecules (*i.e.*, distinguish PCR and sequencing errors from real mutations)." EX1013.0027. Tecan complains that the POSA would not have understood what Bielas meant by "deconvolute." POR at 34-35. The purported dispute about the meaning of "deconvolute" is irrelevant given the anticipating disclosure in the context of Example 3. But to the extent the Board reaches it, the POSA would not have been confused about this word given its use in context in Bielas. As Dr. Sims explained, "deconvolute ... to single molecules" is just another way of saying "deduplicate." EX1079.¶470.

B. Claims 3-4, 6-7, and 10 Are Anticipated By Bielas.

Tecan and Dr. Bustamante do not address these dependent claims. POR at 33-37; EX2035.¶¶141-148. For reasons previously provided, Pet. at 64-65; EX1079.¶¶584-600, ¶¶604-609, these dependent claims are anticipated by Bielas.

C. Claim 9 Would Have Been Obvious Over Bielas

Claim 9 depends from claim 1 and adds that "each unique identifier is 8 nucleotides in length." EX1004 at 26:46-47. Tecan does not address the merits of this claim. *See generally* POR at 33-37; EX2035.¶¶141-148. In any event, Dr.

Bustamante agreed that the POSA would have known it could vary the length of the identifier based on the requirements of any particular experiment. EX1124 at 144:5-145:7; *see also* Pet. at 68-69. Accordingly, claim 9 would have been obvious. EX1079.¶¶601-603.

IV. GROUND I: OBVIOUSNESS OVER IAFRATE AND KIVIOJA

Tecan addresses only claims 1 and 2, POR at 24-30, leaving Dr. Sims' testimony concerning the remaining claims unrebutted. EX1079.¶¶204-253, ¶¶367-393.

A. Claims 1 Would Have Been Obvious.

It bears emphasizing that Dr. Bustamante offered no obviousness opinion about Iafate or Kivioja, nor about the POSA's motivation to combine those references, EX1124 at 157:20-158:1; rather, he addressed the references individually, EX2035.¶¶125-132, ¶¶104-116. There is, moreover, substantial agreement among the parties as to what Kivioja teaches, including that the POSA would have understood Kivioja to use an identifier ("label" in Kivioja) as part of a method of deduplicating sequence reads, EX2035.¶¶114-116; EX1079.¶¶236-240, ¶¶248, ¶¶361-363. The dispute over claim 1 thus comes down to whether the POSA would have understood Kivioja's method to use the "target sequence" in identifying and removing duplicates.

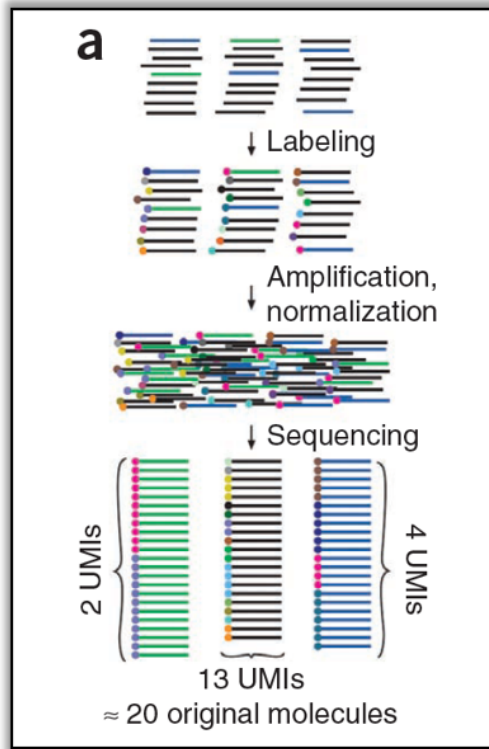
As previously explained, Kivioja started by appending an identifier to fragmented sequences. EX1079.¶238, ¶¶241-242; EX2035.¶¶107-108. After amplification and sequencing, Kivioja used its sequence reads and aligned them to a reference genome. EX1079.¶248; EX2035.¶112. This alignment process, which the POSA would have completed with readily available alignment software like Bowtie, *see, e.g.*, EX1004 at 17:39-47; EX2035.¶56; EX1124 at 139:20-24, resulted in determining a sequence read's position in the genome, i.e., its location (or genomic coordinate) and the associated gene, EX1079.¶248; EX2035.¶113. Kivioja then taught that “the mapped reads with the same gene, position and label were collected to one UMI and the number of such reads was recorded as the copy number of that UMI.” EX1012.0005; EX1079.¶248; EX2035.¶116.

1. Kivioja Taught a Method of Identifying Duplicates that Uses the Target Sequence.

The POSA would have understood that Kivioja's counting method involves identifying duplicates, EX1124 at 150:3-151:18, and that when Kivioja mapped a sequence read to a reference genome, Kivioja used the “target sequence” as described in the '357 patent, EX1004 at 17:39-50; EX1124 at 154:1-155:2; EX1079.¶248, ¶¶274-278, ¶¶361-363. As Dr. Bustamante explained, determining a position in the genome requires that “[t]he sequencing reads,” i.e. the target sequences, EX1004 at 12:45-48, be “aligned to previously generated reference genome sequences,” EX2035.¶¶112-116. The alignment process uses the entire

target sequence, and it certainly uses “at least a portion of the target sequence,” were the Board to adopt that aspect of Tecan’s construction. EX1124 at 139:20-24; EX2035.¶56 (“[T]he alignment tools *compare the nucleotide sequence of each sequencing read* to the nucleotide sequences contained in the reference genome....” (emphasis added)). Dr. Bustamante’s own description of Kivioja’s method cannot be squared with his ultimate conclusion that “[b]ecause Kivioja teaches that the target sequence is only used to identify the gene and position,” the target sequence was “not ... part of the UMI collection process.” EX2035.¶132. As Dr. Bustamante admits, the target sequence is essential to generating coordinates which were then compared to identify duplicates. EX1124 at 150:3-155:2; *see also id.* at 105:24-107:3.

Tecan also cannot explain how Kivioja’s Figure 1(a) (EX1012.0001) shows anything other than a method of identifying and removing duplicates using an identifier and target sequence.



In this figure, the pink circle—an identifier—is appended to both the green and blue sequences. EX1012.0001. Looking at the deduplicated reads at the bottom of the figure, Kivioja’s method was able to distinguish between the pink+green and the pink+blue combinations of identifier and target sequences. EX1012.0001. The method could only have done so by using both the identifier and target sequence. EX1079.¶275. When Dr. Bustamante was asked whether “counting unique molecules involves figuring out which molecules are duplicates and counting them,” he admitted “[i]t involves dealing with duplicate reads one way or another” and confirmed that “as part of the sequencing data processing they [Kivioja] call duplicates.” EX1124 at 150:3-151:8.

2. The POSA Would Have Been Motivated to Modify Iafrate in View of Kivioja.

Dr. Bustamante offered no opinion about the POSA's motivation to combine Iafrate and Kivioja. EX2035; EX1124 at 157:20-158:1. Despite the lack of supporting expert testimony, Tecan nevertheless argues that the POSA would not have been motivated to combine Iafrate and Kivioja. POR at 30-33. Tecan criticizes Petitioner's reliance on Kivioja's teaching that its method could "improve accuracy of almost any next-generation sequencing method," POR at 31, but Dr. Bustamante agreed that Kivioja's method in fact does so, EX1012.0001; EX1124 at 155:3-18, and that the POSA would have understood that to be the case, EX1124 at 155:19-23; *see also id.* at 155:3-158:1. Given Tecan's decision not to provide testimony on this issue from Dr. Bustamante, Dr. Sims' testimony that the POSA would have been motivated to modify Iafrate in view of Kivioja, and would have had a reasonable expectation of success in doing so, stands un rebutted. EX1079.¶¶208-253.

That more than satisfies the Federal Circuit's "flexible" obviousness test. *Intel Corp. v. PACT XPP Schweiz AG*, 61 F.4th 1373, 1379-81 (Fed. Cir. 2023). Arguing otherwise, Tecan cites two PTAB cases for the unremarkable proposition that Petitioner must support "which elements of the cited references could be predictably combined." *Johns Manville Corp. v. Knauf Insulation, Inc.*, IPR2018-00827, Paper 9 at 12 (PTAB Oct. 16, 2018); POR at 31. But that is exactly what Petitioner did. As Dr. Sims explained at length, the POSA would have been

motivated to use Iafrate’s method and improve its accuracy, a problem which Kivioja solved. EX1079.¶¶208-249. Dr. Sims further explained that Iafrate disclosed an adaptor that contained all but one of the elements in claim 1. EX1079.¶211. Dr. Sims also explained that Kivioja disclosed several of the same adaptor elements, including the exact same target sequence primer binding site disclosed in Iafrate, along with the only missing element in Iafrate: the identifier site. EX1079.¶¶242-246. It is simply not the case that Petitioner’s arguments are barebones like those of the petitioners in *Johns Manville* or in *William Wesley*. Compare EX1079.¶¶208-253, with *Johns Manville*, IPR2018-00827, Paper 9 at 11-12, and *William Wesley Carnes, Sr., Inc. v. Seaboard Int’l Inc.*, IPR2019-00133, Paper 10 at 17 (PTAB May 8, 2019) (petitioner offered *no explanation* about why the POSA would have been motivated to combine references or how to combine them). Rather, Petitioner amply satisfied its burden to provide substantial evidence not only that the POSA could have combined Iafrate and Kivioja but “*would have been motivated*” to combine them. See, e.g., *Belden Inc. v. Berk-Tek LLC*, 805 F.3d 1064, 1073-74 (Fed. Cir. 2015); see also EX1079.¶¶208-253.

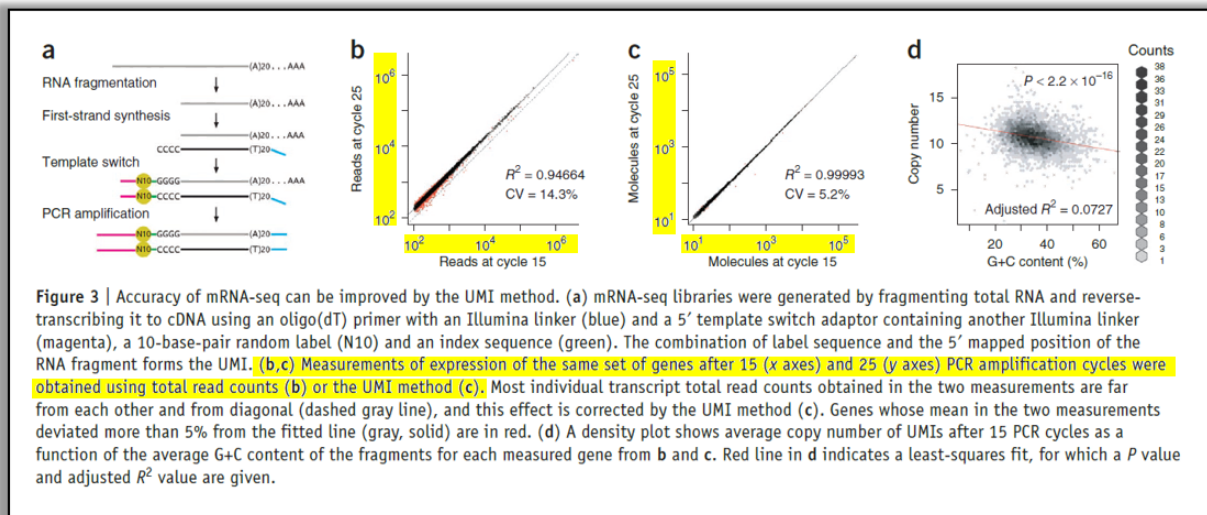
Similarly unavailing are Tecan’s arguments that Petitioner “glosses over the differences between the Iafrate and Kivioja adapters” and is “entirely silent on which aspects of the Iafrate method the POSA would use in any improved sequencing method.” POR at 32. Dr. Sims explained why the POSA would have used Iafrate’s

adaptor in next-generation sequencing, EX1079.¶¶208-224, accuracy issues the POSA might have faced using Iafrate's method, EX1079.¶¶225-235, and how Kivioja's method would have improved the accuracy of Iafrate's method, EX1079.¶¶236-249. Dr. Sims further explained the similarities and differences between the adaptors disclosed in Iafrate and Kivioja and offered an opinion regarding the POSA's reasonable expectation of success in combining the elements of the two adaptors to arrive at the adaptor claimed in the '357 patent. EX1079.¶¶250-253. This extensive, and unrebutted, testimony more than suffices to show that the POSA would have been motivated to combine Iafrate and Kivioja and would have had a reasonable expectation of success in doing so.

B. Claim 2 Would Have Been Obvious.

Tecan and Dr. Bustamante offer conclusory disagreements with Dr. Sims' considered expert opinion. POR at 29-30; EX2035.¶¶133-139. Dr. Bustamante also misdescribes Dr. Sims' testimony. He says that "Dr. Sims ... acknowledges that no duplicate sequencing reads are removed" during Kivioja's procedure. EX2035.¶138. Not so. Dr. Sims testified that, "[f]or example, if a pair of reads each have the same label or molecular tag and the same nucleic acid fragment sequence, *one of them might be removed* in the collapsing process" described in Kivioja. EX2016 at 113:20-114:1 (emphasis added). That process Dr. Sims described "is often referred to as de-duplication." EX2016 at 114:7-9.

At any rate, Tecan is wrong on the merits. Dr. Bustamante opines that “Kivioja does not disclose the removal of any reads” from the UMI groupings. EX2035.¶135. His opinion stands in contrast to Kivioja’s disclosures, EX1012.0005 (duplicates “collected to one UMI”); EX1012.0001 (“[T]he number of original DNA molecules can be determined simply by counting each UMI only once.”), and Dr. Sims’ testimony, EX1079.¶248, ¶¶239-240, ¶285. Moreover, Figures 3(b) and 3(c) in Kivioja, EX1012.0002, report a significant reduction in sequence reads through the use of Kivioja’s UMI (or deduplication) method:



As highlighted in the annotated version above, Figure 3(b) depicts post-sequencing read counts for a set genes. EX1012.0002. Figure 3(c) depicts the same data after performing deduplication with Kivioja’s UMI method. EX1012.0002. Comparing the number of reads, and scales on the x- and y-axes in both Figures, there is a roughly 10-fold reduction in sequences using the UMI method of

deduplication. EX1012.0002. Kivioja illustrates similar data in Supplementary Figure 4. EX1012.0010. Kivioja thus discloses the removal of duplicate sequencing reads from a population of identified duplicates.

C. Claims 3-4, 6-7, and 9-10 Would Have Been Obvious

Tecan and Dr. Bustamante do not address these dependent claims. POR at 24-33; EX2035.¶¶106-116, ¶¶125-140. For reasons previously provided, these dependent claims would have been obvious over Iafrate and Kivioja. Pet. at 24-47; EX1079.¶¶204-253, ¶¶367-393.

V. TECAN’S DISCLAIMER OF THE RELATED PATENTS

IDT filed petitions challenging the patentability of claims in two patents related to the ’357 patent, specifically, IPR2024-01502 and IPR2024-01506. After the Board instituted review of these petitions, Patent Owner opted not to defend these proceedings, filing statutory disclaimers of all challenged claims. The Board accordingly terminated and issued adverse judgments. *See* IPR2024-01502, Paper 23 (Aug. 11, 2025); IPR2024-01506, Paper 23 (Aug. 12, 2025).

It bears emphasis that the Examiner had concluded that certain of the ’357 patent’s claims were not patentably distinct from U.S. Patent No. 9,946,399. EX1019.0404-08. The claims issued only because Tecan filed a terminal disclaimer. EX1019.0465, .0441-43. That terminal disclaimer is a “strong clue that a patent examiner and, by concession, the applicant, thought the claims in the continuation

lacked a patentable distinction over the parent.” *SimpleAir, Inc. v. Google LLC*, 884 F.3d 1160, 1168 (Fed. Cir. 2018).

While the Board should not cancel the claims challenged here simply because of these adverse judgments, *see SoftView LLC v. Apple Inc.*, 108 F.4th 1366, 1372 (Fed. Cir. 2024), the Board can, and should, take note that Patent Owner’s Response offers no analysis that purported to distinguish the ’357 patent from its disclaimed patents. As shown above, this dispute now turns solely on how the prior art taught and rendered obvious a method that “identif[ies] sequence reads with identical identifier and target sequences as duplicates.” U.S. Patent No. 11,725,241, at issue in IPR2024-01506, claimed methods *with the exact same limitation*. Compare EX1004 at 25:46-47, *with* EX1005 at 25:42-43. The Board should not uphold the validity of method claims based on the “identifying” limitation while indistinct claims have been disclaimed.

CONCLUSION

Petitioner respectfully requests that the Board cancel claims 1-4, 6-7, and 9-10 of the ’357 patent.

Dated: November 3, 2025

Respectfully submitted,

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Integrated DNA Technologies, Inc.

CERTIFICATION UNDER 37 C.F.R. § 42.24(d)

I hereby certify that the foregoing complies with the type-volume limitations of 37 C.F.R. § 42.24(d) and contains 5,600 words, excluding those portions exempted under 37 C.F.R. § 42.24(a)(1).

/Thomas S. Fletcher/
Thomas S. Fletcher
Reg. No. 72,383

CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 42.6(e) and 37 C.F.R. § 42.105, I hereby certify that on November 3, 2025, I caused the foregoing Petitioner's Reply Brief, Exhibit List, and the accompanying exhibits to be served on Patent Owner by electronic mail to Linnea P. Cipriano, Scott T. Weingaertner, John P. Padro, and Timothy J. Beavers, at DG-GoodwinTecan@goodwinlaw.com, counsel for Plaintiffs in *Tecan Genomics, Inc. v. Invitae Corp. et al.*, C.A. No. 23-cv-1114-GBW (D. Del.).

Dated: November 3, 2025

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